thereby prevent relapse of the small cell lung cancer in the subject.--

REMARKS

Claims 1-16 are pending in the subject application. Applicants have hereinabove canceled claims 3-4 and 9-10 without prejudice or disclaimer to applicants right to pursue the subject matter of these claims in a later-filed application and amended claims 1, 5-7, 11-12, 14 and 16. Support for these amendments may be found inter alia in the specification as follows: claim 1, page 10, lines 4-16; claims 12, 14 and 16: page 11, lines 24-28 . This amendment does not involve any issue of new matter. Therefore, entry of this amendment is respectfully requested such that claims 1-2, 5-8 and 11-16 will be pending.

Rejection under 35 U.S.C. 112, first paragraph

The Examiner rejected claims 12-16 are under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Examiner stated that claims 12-16 are rejected under 35 U.S.C. §112, first paragraph, because the specification while being enabling for eliciting an immune response against small cell lung cancer cells, does not reasonably provide enablement for all cancers. The Examiner stated that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The Examiner stated that the claims are drawn to a method of preventing and treating cancer by administering a fucosyl GM1

ganglioside conjugated to am immunogenic carrier, KHL and formulated with an adjuvant such that an antibody response in stimulated. The Examiner stated that an effective therapeutic or preventative protocol for the treatment or prevention of the formation of a tumor is subject to a number of factors which enter the picture beyond simply the specific binding of an antibody to the tumor cell line derived antigen. The Examiner stated that demonstrating tumor antigen specificity in vitro cannot alone support the predictability of the method for prevention of or treating said tumor growth through administration of either the antibody or T cell line expressing the appropriate specificity. The establishment and growth of a tumor is subject to variables beyond antigen specificity. The Examiner stated that the ability of a host to suppress and thereby prevent the tumor from establishing itself will vary depending upon factors such as the condition of the host, the type of tumor (rapidly proliferating or slowly proliferating) and the tumor burden. The Examiner stated that thus, it is unpredictable as to the protective nature of the fucosyl GM1 ganglioside vaccine or immunogen. The Examiner stated that the specification merely provides results of a safety and immunogenicity study that indicated that antibodies of bot IgM and IgG class were detected in the sera of volunteers. The Examiner stated that the study was done in patients who already has suffered from SCLC or were suffering from SCLC. The Examiner stated that the Examiner stated that it is not clear if there were antibodies existing in such patients (Grazyna et al, 1996 Immunol. Letters, vol 52 (2,3) pgg. 89-93 teach that auto antibodies to fucosylated GM1 are present in patients) and whether the presence of such antibodies already indicated that therapeutic effects may not be achievable. The Examiner stated that no working examples have been

provided that would guidance to one of skill in the art that the method of the inventions can be practiced without undue experimentation. The Examiner stated that with respect to preventing and treating other cancers, there is no guidance or teaching provided to one skilled in the art as to the vast numbers of tumours/cancers that can be treated or prevented by this method, The Examiner stated that it appears that SLC are the only cancers that the invention is drawn to. The Examiner stated that no clear evidence is available during a search in the literature data base that Fuc-GM1 ganglioside is a protective antigen in other types of cancers. The Examiner stated that since there are also naturally occurring cell membrane antigens, it is not clear how a treatment or prevention can be envisioned. The Examiner stated that the specification also does not provide any guidance as to how to select or apply the methods to a subject in whom prevention can be monitored. The Examiner stated that how does a person or ordinary skill in the art select a candidate, immunize the candidate with the immunogen of the invention and then monitor if cancer has been prevented because it is not a predictable phenomena as to which individual will definitely get cancer. The Examiner stated that for all the reasons above, one skilled in the art cannot practice the claimed invention.

In response, applicants respectfully traverse the Examiner's above rejection. Nevertheless, applicants without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application have herein amended claims 12, 14 and 16 to recite small cell lung cancer, as the Examiner has conceded that the specification is enabling for eliciting an immune response against small cell lung cancer cells. Applicants contend that this

amendment obviates the above rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejection under 35 U.S.C. §103 (a)

The Examiner rejected claims 1-11 under 35 U.S.C. 103 (a) as being unpatentable over Jennemann et al (1996) and Vangsted et al (1994) in view of Kensil et al (1991). The Examiner stated that this same rejection may also apply to claims 12-16 if Applicant can successfully counter the 112, first paragraph rejection set forth above.

The Examiner stated that Jenenmann et al teach that optimal mode of vaccination with fucosylated ganglioside conjugated to KHL was able to stimulate high antibody levels in the presence of an adjuvant such as MPL-A. The Examiner stated that Vangsted et al teach that Fuc GM1 is a target for ADCC. The Examiner stated that Jennemann et al do not teach adjuvants such as the claimed saponin , Quill A or QS-21. The Examiner stated that Kensil et al teach the use of the adjuvant derived from the bark of Qillaja saponaria Molina tree (from which QS-21 is derived) as efficient and safe adjuvants. The Examiner stated that it would have been prima facie obvious to a person of ordinary skill in the art at the time of the claimed invention to combine the teachings of Jennemann and Kensil to arrive at the claimed invention as the prior art in combination provided the motivation and a reasonable expectation of success at obtaining an enhanced antibody production to immunization with Fuc-GM1-KLH formulated in an adjuvant.

In response, applicants respectfully traverse the Examiner's above

Exhibit A

--1. (Amended) A composition [comprising] which comprises:

a) a conjugate of i) a fucosyl GM1 ganglioside derivative [or a oligosaccharide portion thereof conjugated] to ii) an immunogenic protein,

b) [an adjuvant] a carbohydrate derived from the bark of a Quillaja saponaria Molina tree, and

c) a pharmaceutically acceptable carrier,

the amounts of such conjugate[d ganglioside] and such adjuvant being effective to stimulate or enhance antibody production in a subject, [and a pharmaceutically acceptable carrier] wherein, in the conjugate the ganglioside derivative is conjugated to the immunogenic protein through a ceramide portion of the ganglioside.--

--5. (Amended) The composition of claim [4] 1, wherein the carbohydrate is QS-21.--

--6. (Amended) The composition of claim 1, wherein the amount of the ganglioside is an amount between about 3 μg [to] and about 100 μg.--

--7. (Amended) The composition of claim 5, wherein the amount of QS-21 is an amount between about 30 μg [to] and about 100 μg.--

--11. (2X Amended) A method of enhancing antibody production in

a subject which comprises administering to the subject an effective antibody producing amount of the composition of claim 1, [effective to enhance antibody production in the subject,] so as to thereby enhance antibody production in the subject.--

--12. (2X Amended) A method of preventing a small cell lung cancer in [the] a subject which comprises administering to the subject an effective small cell lung cancer preventing amount of the composition of claim 1, [effective to prevent cancer] so as to thereby prevent the small cell lung cancer in the subject.--

--14. (2X Amended) A method of treating a small cell lung cancer in a subject which comprises administering to the subject an effective small cell lung treating amount of the composition of claim 1, [effective to treat cancer] so as to thereby treat the small cell lung cancer in the subject.--

--16. (Amended) A method of preventing relapse of a small cell lung cancer [cancer] in a subject which comprises administering to the subject an effective small cell lung cancer relapse preventing amount of the composition of claim 1, so as to thereby prevent relapse of [a] the small cell lung cancer in the subject.--